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EXCITATION RATIOMETRIC FLUORESCENT BIOSENSOR FOR ZINC ION AT PICOMOLAR LEVELS

[0001] This application claims priority to U.S. Provisional Application Nos. 60/414,657 filed on October 1, 2002 and 60/416,515 filed October 8, 2002 under 35 U.S.C. § 119(e), the contents of which are herein incorporated by reference.

FIELD OF THE INVENTION

[0002] The present invention relates to a biosensor for measurement of zinc ion in a sample. The invention provides compositions and methods for measuring zinc ion at picomolar concentrations *in vitro* and *in vivo*.

BACKGROUND OF THE INVENTION

[0003] Zinc is an ion of growing importance in many fields of biology and medicine. In particular, recent work has demonstrated the excitotoxic role(s) of zinc in the brain, [1-3] as well as its potential role as a signaling ion in the brain [4] which recent evidence suggests participates in long term potentiation [5]. Elsewhere in the body, zinc seems to play a role in the immune response [6], and is a prevalent constituent of semen, as well as an essential cofactor in many enzymes [7] and the ubiquitous "zinc fingers" of transcription factors [8]. The role of zinc in apoptosis is the subject of controversy [9], and there is no consensus as to how zinc is distributed in the body, allocated amongst its many role(s), or how these processes are regulated. The availability of selective, sensitive, quantifiable fluorescent calcium indicators beginning with Quin-2, Fura-2, and Indo-1 [10] has revolutionized our understanding of calcium, and if analogous indicators were available for zinc, perhaps comparable progress could be made. Despite substantial effort [9, 11-16], it is only recently that fluorescent zinc indicators have been made which offer adequate selectivity over potential interferents such as Ca and Mg; reliable quantitation through intensity ratios, anisotropy, or fluorescence lifetime; and useful sensitivity. In particular, the recently introduced FuraZin-1 and Newport Green DCF from Molecular Probes offer selectivity